IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Dean L. Engelhardt et al.	
Serial No.	08/479,997	Group Art Unit: 1634
Filed:	June 7, 1995	Exam'r: Scott W. Houtteman
Title:	OLIGO- OR POLYNUCLEOTIDES, AND OTHER OTHER COMPOSITIONS COMPRISING PHOSPHATE MOIETY LABELED NUCLEOTIDES	

Dearborn, Michigan

Honorable Commissioner of Patents and Trademarks
The United States Patent and Trademark Office
Washington, D.C. 20231

DECLARATION OF DR. ANN SODJA
(IN SUPPORT OF THE NON-OBVIOUSNESS OF THE INVENTION CLAIMED IN U.S. PATENT APPLICATION SERIAL NO. 08/479,997)

I, Ann Sodja, hereby declare as follows:

1. I am presently Associate Professor in the Department of Biological Sciences at Wayne State University, Detroit, Michigan, having been appointed such in 1982. Under Dr. Paul K. Stumpf, my advisor, I received my doctorate in biochemistry from the University of California, Davis, California in 1974. My doctoral thesis was titled "Metabolism of Medium Chain Length Fatty Acids in Higher Plants." Earlier in 1964, I had received a Masters of Science in biochemistry from the Ohio State University, Columbus, Ohio. Prior to that, I had received an A.B. in chemistry with honors from Ursuline College, Cleveland, Ohio 1962. From 1974 through 1978, I was a post-doctoral fellow at California Institute of Technology in Pasadena, California, where I conducted research involving several gene families of *Drosophila melanogaster*. In particular, I worked on 5S RNA and tRNA genes, and techniques for their enrichment and mapping by electron microscopy. Dr. Norman Davidson was my post-doctoral mentor. It was also there that I initiated research on actin genes of *Drosophila melanogaster* and I continued that research for several years. In addition to presently being a tenured professor at Wayne State University, my professional appointments have included being appointed Associate Professor at WSU in 1982 and Assistant Professor at WSU in 1978. My academic background

and professional experience are listed on my curriculum vitae (CV) attached to this Declaration as Exhibit 1.

2. Among my honors and awards are the following: Charles Kettering Predoctoral Fellowship, 1962-1963; NIH Predoctoral Traineeship, 1963-1965; Max-Planck Fellowship for Visiting Scientists, 1967-1968; NSF Predoctoral Fellowship, 1969-1974; American Cancer Society Postdoctoral Fellowship, California Division, 1974-1976; Research Fellow in Chemistry, California Institute of Technology, 1976-1978; Career Development Chair Award, WSU, 1984; Presidential Excellence Award, WSU, 1986, 1987 & 1990; and Women of Wayne Staff/Faculty Recognition Award, honorable mention, 1989. I was also nominated by the students for the President's Award for Excellence in Teaching in 1990 and 1991. These and other professional honors and awards are listed on my CV (Exhibit 1).

3. I am the author of several scientific publications, including a number of published investigations dealing with the genetics and biochemistry of *Drosophila melanogaster* and its actin gene. These publications, including submitted publications and publications in preparation, number more than twenty and are listed on my CV (Exhibit 1). I have also published an equal number of abstracts which are listed on my CV (Exhibit 1). I have also authored five book reviews and other published materials as listed on my CV (Exhibit 1). In addition, I have presented thirty posters including eleven oral posters and nineteen poster presentations. I have given talks at more than two dozen seminars where I was invited to speak. These are also listed on my CV (Exhibit 1). Other professional experience including my professional memberships, fellowships and grants, faculty research and special awards, committee assignments, professional consultations, journal and editorial activities and other professionally related services are all listed on my CV (Exhibit 1).

4. Among my scientific publications is the Sodja and Davidson 1978 article published in Nucleic Acids Research (volume 5, pages 385-401) and titled "Gene Mapping and Gene Enrichment by the Avidin-Biotin Interaction: Use of Cytochrome-c as a Polyamine Bridge." A copy of my 1978 Nucleic Acids Research article is attached as Exhibit 2. In my investigation of the biochemistry and genetics of arthropods, including *Drosophila melanogaster*, spanning more than

three decades, I have examined nucleic acids, including DNA from a number of different species using a number of different and diverse formats. I am thoroughly familiar with nucleic acid detection formats and nucleic acid probe technology, having spent the better part of my professional career exploring their use as investigative tools for genetic analyses in arthropods and other species.

5. I have been engaged by Enzo Biochem, Inc. as a scientific consultant in order to review portions of the current prosecution of U.S. Patent Application Serial No. 08/479,997 ("Oligo- or Polynucleotides And Other Compositions Comprising Phosphate Moiety Labeled Nucleotides") that was filed on June 7, 1995. I am being compensated as a consultant by Enzo for this review and for making this Declaration. Included for my review were significant portions of the file wrapper for this application, including the original specification (hereinafter "the '997 specification"), the previously pending claims in this application (454-575), changes to independent claims (454, 482, 511 and 539)[1] to be submitted in a response (Amendment Under 37 C.F.R. §1.116) to the July 18, 2000 Office Action, and the latest composite set of claims (454-567) which will be pending in this application following the submission of the aforementioned Amendment After Final. A copy of the previously pending claims (454-575), the changes to the independent claims (454, 482, 511 and 539), and the latest composite set of claims (454-567) are attached to this Declaration as Exhibits 3, 4 and 5, respectively. I also understand that this Declaration will be submitted in connection with that aforementioned Amendment to be filed with the U.S. Patent and Trademark Office. I have also reviewed the July 18, 2000 Office Action as well as five other previous Office Actions issued on June 20, 1996, May 13, 1997, January 6, 1998, September 29, 1998 and February 3, 1999. I have also reviewed several papers filed in response to the aforementioned office actions. These papers include Applicants' June 23, 2000 Communication, their June 22, 2000 Second Supplemental Amendment, their June 20, 2000 Supplemental Amendment, their January 4, 2000 Amendment Under 37 C.F.R. §1.115, their January 19, 1999 Supplemental Response, their November 20, 1998 Amendment Under 37 C.F.R. §1.116, their July 6, 1998 Amendment Under 37 C.F.R. §1.115, their November 24, 1997 Amendment Under 37 C.F.R. §1.116, and their

[1] **I understand that several dependent claims have also been amended. The affected dependent claims include 455, 459, 461, 466, 476, 480, 483, 487, 489, 494, 504, 508, 510, 512-531, 533, 535-559, 561 and 563-567. I have also reviewed the amendments to the dependent claims which will also be submitted in Applicants' January 18, 2001 Amendment Under 37 C.F.R. §1.116.**

December 20, 1996 Amendment In Response To June 20, 1996 Office Action And Request For A Three Month Extension Of Time. I generally agree with the substance of Applicants' remarks and positions as set forth in these aforementioned responses, including those set forth in the Declaration of Dr. Dean L. Engelhardt In Support Of Adequate Description and Enablement that was submitted as Exhibit A to Applicants' November 27, 1997 Amendment Under 37 C.F.R. §1.116 In Response To June 25, 1997 Office Action. I have also reviewed the Examiner Interview Summary Records dated November 3, 1998 and August 24, 2000. As the author, I am very familiar, of course, with the publication, Sodja and Davidson (1978) ["Gene Mapping and Gene Enrichment by the Avidin-Biotin Interaction: Use of Cytochrome-c as a Polyamine Bridge," Nucleic Acids Research 5:385-401 (1978)] (Exhibit 2), that in combination with another publication [Gohlke et al., U.S. Patent No. 4,378,458, issued on March 29, 1983, based on an application first filed on March 30, 1981] was cited in several office actions for obviousness by the U.S. Patent Examiner against the various pending claims in this application. A copy of the Gohlke '458 Patent is also attached to this Declaration as Exhibit 6.

6. I understand that in the latest July 18, 2000 Office Action claims 454-575 were rejected under 35 U.S.C. §103 for being unpatentable over Gohlke et al., U.S. Patent No. 4,378,458 (Gohlke '458 Patent), issued on March 29, 1983, based on an application filed on filed March 20, 1981, in view of Sodja et al., Nucleic Acids Research 5(2):385-401 (1978) and further in view of applicant's admissions for reasons of record. I further understand that in the previous February 3, 1999 Office Action, the same claims were also rejected under 35 U.S.C. §103 for being unpatentable over the Gohlke '458 Patent in view of Sodja et al. (1978) and further in view of applicant's admissions. In the February 3, 1999 Office Action (page 5), the Examiner stated:

> Applicant argues that the opening of the ring sugar in Sodja distinguishes Sodja from the claims of the current application. It is argued that the terminal nucleotide, with the open sugar, is outside the scope of the claims.
>
> This argument is not persuasive. Sodja reads on the claimed invention because of the scope of the term "SIG" moiety. There is nothing in the limitation "SIG" which would exclude the terminal nucleotide, with the open ribose sugar from being part of the "SIG" moiety. The "terminal" nucleotide in the claimed product would be the second nucleotide from the end in the Sodja reference, which has a closed sugar ring.

> Applicant argues that Gohlke does not teach labeling ribonucleotides and thus does not suggest the claimed DNA products. This argument is not persuasive. First, many of the claims of this case are not limited to DNA products but read on ribonucleotides. Second, it is Gohlke in view of Sodja which is the basis of the rejection. There is no evidence that Gohlke cannot be applied to Sodja for the expected benefit of generating other types of labeled oligonucleotides using the Gohlke labels.

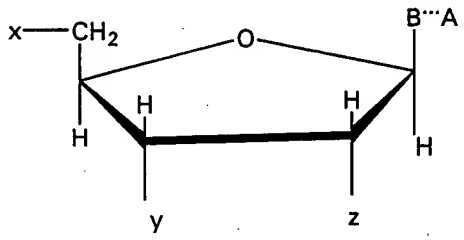
7. Based upon my review, I understand that the claimed invention is directed to detectable nucleic acid compositions, i.e., oligo- or poly(deoxyribo)nucleotides, comprising at least one modified nucleotide.

A. As set forth in amended claim 454 (Exhibit 4), one significant embodiment as I understand it is an oligo- or polydeoxynucleotide which is complementary to a nucleic acid of interest or a portion thereof. The oligo- or polydeoxynucleotide comprises at least one modified nucleotide having the formula

Sig—PM—SM—BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof. The PM is attached to SM, the BASE is attached to SM, and Sig is covalently attached to PM directly or through a chemical linkage. The element Sig comprises a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when the modified nucleotide is incorporated into the oligo- or polydeoxynucleotide or when the oligo- or polydeoxynucleotide is hybridized to the complementary nucleic acid of interest or a portion thereof.

B. As set forth in amended claim 482 (Exhibit 4) and as I understand it, another significant embodiment of the claimed invention is an oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof. The oligo- or polydeoxyribonucleotide comprises at least one modified nucleotide having the structural formula:



In the structural formula, BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and is attached to the 1′ position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine. The substituents x, y and z are selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate. Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof. Sig comprises a non-radioactive label moiety which can be directly or indirectly detected when so attached to the phosphate or when the modified nucleotide is incorporated into the oligo- or polydeoxynucleotide or when the oligo- or polydeoxynucleotide is hybridized to the complementary nucleic acid of interest or a portion thereof.

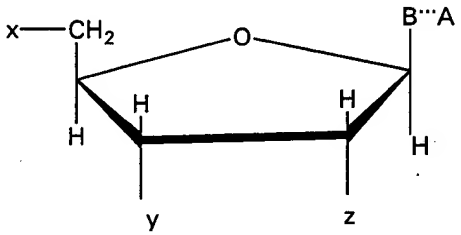
C. I understand that the claimed invention as set forth in amended claim 511 (Exhibit 4) is directed to an oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof. The oligo- or polynucleotide comprises at least one modified nucleotide having the formula

Sig – PM – SM – BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof. PM is attached to SM, BASE is attached to SM, and Sig is covalently attached to PM directly or via a chemical linkage. Sig comprises a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when the modified nucleotide is incorporated into the oligo- or polynucleotide, or when the oligo- or polynucleotide is hybridized to the complementary nucleic acid of interest or

a portion thereof. When the oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, the chemical linkage in this oligo- or polynucleotide is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to the oligoribonucleotide or polyribonucleotide.

D. I understand another embodiment as set forth in amended claims 539 (Exhibit 5) is an oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof. The oligo- or polynucleotide comprises at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine. The elements x, y and z are selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate. Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof. Sig comprises a non-radioactive label moiety which can be directly or indirectly detected when so attached to the phosphate or when the modified nucleotide is incorporated into the oligo- or polynucleotide, or when the oligo- or polynucleotide is hybridized to the complementary nucleic acid of interest or a portion thereof. Furthermore, when the oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, the chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucl otide previously attached to the oligoribonucleotide or

polyribonucleotide.

8. As Enzo's consultant and on its behalf, I am making this Declaration in support of the non-obviousness of the claims in this application which will be pending after submission of Applicants' Amendment Under 37 C.F.R. §1.116. To the extent that the subject matter is similar with those of the previously pending claims prior to submission of Applicants' Amendment, my remarks are applicable to those previously pending claims prior to the latest amendments as well.

9. Based upon my own training, background and experience, I would submit that at the time this application was first filed in June 1982, a person of ordinary skill in the art relevant to the subject matter being claimed, including nucleic acid modification, synthesis, hybridization and detection, would have possessed or could have been actively pursuing an advanced degree in organic chemistry and/or biochemistry. Such an ordinarily skilled person could also be at least approaching or ranging toward the level of a junior faculty member with 2-5 years of relevant experience, or would at least be a postdoctoral student with several years of experience. I consider myself to possess the level of skill and knowledge of at least a person of ordinary skill in the art to which the present application and invention pertains.

10. As a person of at least ordinary skill in the art to which the present invention pertains, it is my opinion and conclusion that the subject matter of claims 454-567 would not have been rendered obvious at the time the invention was made from a combined reading of the Gohlke et al. (U.S. Patent No. 4,378,458) in view of Sodja et al. [Nucleic Acids Research 5(2):385-401 (1978)] and further in view of applicant's admissions for reasons of record. My reasons why the invention set forth in claims 454-567 would have been non-obvious are set forth in the paragraphs below.

11. As the author of the cited Sodja and Davidson (1978) (Exhibit 2), I wish to point out that our work was intended to help us with electron microscopic gene mapping and gene enrichment of DNA:RNA hybrids. By coupling cytochrome-c to the oxidized 2', 3' terminus of RNA and attaching biotin labels to the coupled cytochrome-c, we found that electron microscopic gene mapping could be carried out efficiently with avidin-ferritin and avidin-polymethacrylate sphere labels. For

our gene mapping studies, Dr. Davidson and I used DNA and RNA from *E.* coli and *Drosophila melanogaster*. Examples of our results obtained with this method are shown by the electron micrographs in Figures 2 and 4 which are published in our 1978 paper (Exhibit 2) on pages 393 and 396, respectively. Furthermore, we found that gene enrichment was also efficiently obtained by buoyant banding of DNA:RNA-biotin:avidin-spheres in cesium chloride (CsCl) gradient. Results of our enrichment experiments for 5S rRNA from Drosophila DNA are presented in Table II on page 398 in my 1978 paper (Exhibit 2).

12. At the time when I was conducting experiments related to my 1978 paper, I was neither thinking nor intending to attach a detectable non-radioactive label to the terminus of RNA for the purpose of making a nucleic acid hybridization probe. Rather, after hybridizing the modified RNA with DNA, I was using large marker molecules, such as avidin-ferritin and avidin spheres, to produce more efficient gene mapping by electron microscopy and gene enrichment by cesium chloride gradient. In my work, we oxidized the free 2', 3' OH groups of RNA to the dialdehyde form using periodate. This is described in my 1978 paper both in the reaction scheme outlined on page 386 (no. 1) and in the MATERIALS AND METHODS Section on page 387 under Preparation and Purification of RNA-Cytochrome-c:

> tRNA or 5S RNA were heated at 80° for 1-8 min in 1 mM NaAc buffer at pH 6.8, cooled, adjusted to 0.1 M NaAc buffer (pH 4.8) and treated with periodate as previously described (1). The amount of RNA used was 0.5 - 1 mg in 0.5 - 1 ml of reaction mixture.

The publication cited as (1) above is Broker et al., "Electron microscopic visualization of tRNA genes with ferritin-avidin:biotin labels," also in Nucleic Acids Research, 5(2):363-384 (1978). A copy of Broker et al. is attached to my Declaration as Exhibit 7.

13. As a person of ordinary skill in the art, I wish to point out that the periodate oxidation method used in my 1978 paper (Exhibit 2) and in Broker et al. (Exhibit 7) is applicable only to RNA which has two vicinal OH groups at the 3' and 2' positions. Other nucleic acids, including DNA, do not possess an OH group on the 2' position. Thus, the periodate oxidation method used in my 1978 paper (Exhibit 2) or Broker et al. (Exhibit 7) could not be used to attach a detectable non-

radioactive label to DNA as set forth, for example, in claims 454 and 482 (see amendments to independent claims (Exhibit 4) and composite set of claims (Exhibit 5) in this application.

14. As a person of ordinary skill in the art, it is my opinion and conclusion that the claims 511 and 539 in this application, which claims are drawn to an oligo- or polynucleotide, are outside of our 1978 paper (Exhibit 2) or Broker et al. (Exhibit 7). As set forth in Paragraph 7C and 7D above, the amendments to the independent claims (Exhibit 4) and the composite set of claims, claims 511 and 539 contain the proviso that

> . . . provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3′ terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

Clearly, the fact that claims 511 and 539 eschew any and all chemical linkages which are obtained through a 2',3' vicinal oxidation of a terminal ribonucleotide, is significant because my 1978 paper relied exclusively on the vicinal oxidation of RNA using periodate. It is my opinion and conclusion that the subject matter of claims 511 and 539 would not have been taught or suggested to one of ordinary skill in the art at the time this application was first filed in June 1982 from reading my 1978 paper (Exhibit 2), taken with Gohlke's '458 Patent (Exhibit 6) and any of Applicants' admissions of record. As previously stated, the chemistry disclosed in my 1978 paper relied exclusively on vicinal oxidation of the free 2, 3' OH groups of RNA. The subject matter set forth in claims 511 and 539 clearly avoids such chemistry.

15. At the time that I conducted the experiments disclosed in my 1978 paper, I was concerned that the chemistry would not work with oligoribonucleotides (10 ribonucleotides or less) or very short polyribonucleotides. With such short pieces of RNA, I felt at the time that the addition of a large linker, such as cytochrome c, and a large biotin marker, might be too large in comparison to the length of the RNA such that steric hindrance would reduce, if not stymie hybridization between complementary RNA and DNA strands altogether.

16. I understand that in the obviousness rejections made in both the February 3, 1999 and July 18, 2000 Office Actions, the Gohlke '458 Patent was cited as the primary reference, and my 1978 paper as the secondary reference. This was explained on page 5 in the February 3, 1999 Office Action:

> it is Gohlke in view of Sodja which is the basis of the rejection. There is no evidence that Gohlke cannot be applied to Sodja for the expected benefit of generating other types of labeled oligonucleotides using the Gohlke labels.

It is my opinion and conclusion that even applying Gohlke's disclosed labels to my 1978 paper, one of ordinary skill in the art would not have arrived at the claimed invention in this application, as set forth in claims 454-567. As stated earlier, the chemistry used in my 1978 paper could not be applied to nucleic acids, such as DNA that lacked the 2' OH group otherwise found in RNA. Moreover, the claims drawn to the use of a terminal ribonucleotide as a modified nucleotide specifically avoid the vicinal oxidation and periodate chemistry described in my 1978 paper. Thus, using Gohlke's labels with the chemistry from my 1978 paper, one of ordinary skill in the art would not have arrived at the invention now claimed in this application. Nor, would such a person have had a reasonable expectation of success in reaching the present invention from a combined reading of Gohlke's 458 Patent, my 1978 paper and any statements made by the Applicants which are of record in this application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of the application or any patent issued thereon.

17/I/2001
Date

Ann Sodja Ph.D.
Ann Sodja, Ph.D.

* * * * * * *

Declaration.AS.1.17.01

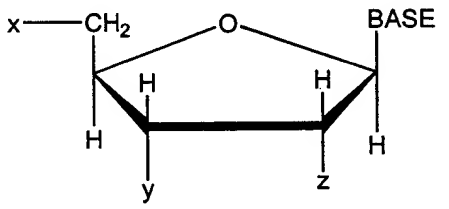
Enz-5(D6)(C2)

454. (Amended) An oligo- or polydeoxynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxynucleotide comprising at least one modified nucleotide having the formula

Sig—PM—SM—BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or through a chemical linkage, said Sig [being a moiety capable non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

482. (Amended) An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

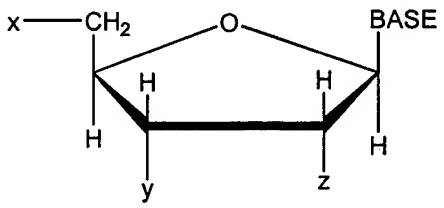
wherein Sig is covalently attached [to x, y or z] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig [being a moiety capable of non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to [x, y or z] said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

511. (Amended) An oligo- or [polyribonucleotide] polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one [ribonucleotide] modified nucleotide having the formula

Sig – PM – SM – BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM [at a position of SM selected from the 2', 3' and 5' positions, or combinations thereof], said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig [being a moiety capable of non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or [polyribonucleotide] polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not [a cleaved 3' terminal ribonucleotide] obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said [oligo- or polyribonucleotide] oligoribonucleotide or polyribonucleotide.

539. (Amended) An oligo- or [polyribonucleotide] polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1′ position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached [to x, y or z] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig [being a moiety capable of non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to [x, y or z] said phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to [y of] a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not [a cleaved 3' terminal ribonucleotide] obtained through a 2',3' vicinal oxidation of a 3′ terminal ribonucleotide previously attached to said [oligo- or polyribonucleotide] oligoribonucleotide or polyribonucleotide.

454. An oligo- or polydeoxynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxynucleotide comprising at least one modified nucleotide having the formula

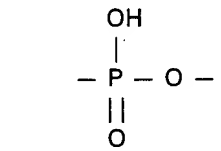
Sig—PM—SM—BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or through a chemical linkage, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

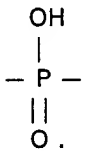
455. The oligo- or polydeoxyribonucleotide of claim 454, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

456. The oligo- or polydeoxyribonucleotide of claim 454, wherein said Sig moiety comprises at least three carbon atoms.

457. The oligo- or polydeoxyribonucleotide of claim 454, wherein said covalent attachment is selected from the group consisting of



and



458. The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

459. The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

460. The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage comprises an allylamine group.

461. The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties:

$$-CH=CH_2-NH-$$

$$-CH=CH-CH_2-NH-$$

$$-CH=CH-CH_2-O-CH_2-\underset{\underset{OH,}{|}}{CH}-CH_2-NH-,$$

$$-S-,\quad -\overset{\overset{O}{||}}{C}-O, \text{ and } -O-.$$

462. The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

463. The oligo- or polydeoxyribonucleotide of claim 454, wherein said PM is monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or phosphate oyxgen.

464. The oligo- or polydeoxyribonucleotide of claim 454, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme or an enzyme component, a hormone or a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten and an antibody or an antibody component, or a combination of any of the foregoing.

465. The oligo- or polydeoxyribonucleotide of claim 464, wherein said electron dense component comprises ferritin.

466. The oligo- or polydeoxyribonucleotide of claim 454, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein.

467. The oligo- or polydeoxyribonucleotide of claim 464, wherein said magnetic component comprises magnetic oxide.

468. The oligo- or polydeoxyribonucleotide of claim 467, wherein said magnetic oxide comprises ferric oxide.

469. The oligo- or polydeoxyribonucleotide of claim 464, wherein said enzyme or enzyme component is selected from the group consisting of alkaline phosphatase, acid phosphatase, β-galactosidase, ribonuclease, glucose oxidase and peroxidase.

470. The oligo- or polydeoxyribonucleotide of claim 464, wherein said metal-containing component is catalytic.

471. The oligo- or polydeoxyribonucleotide of claim 464, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

472. The oligo- or polydeoxyribonucleotide of claim 464, wherein Sig is selected from the group consisting of an antigen or hapten capable of complexing with an antibody or antibody component specific thereto, and an antibody or antibody component capable of complexing with an antigen or hapten.

473. The oligo- or polydeoxyribonucleotide of claim 454, wherein said oligo- or polydeoxyribonucleotide is terminally ligated or attached to a polypeptide.

474. A composition comprising th oligo- or polydeoxyribonucleotide of claim 454, a polypeptide capable of forming a complex with Sig and a moiety which can be detected when such complex is formed.

475. The composition of claim 474, wherein said polypeptide comprises polylysine.

476. The composition of claim 474, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

477. The composition of claim 474, wherein said Sig is a ligand and said polypeptide is an antibody thereto.

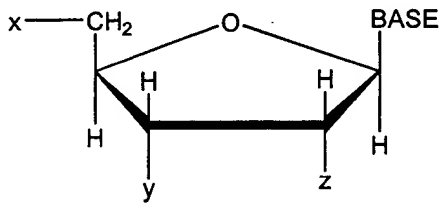
478. The oligo- or polydeoxyribonucleotide of claim 454, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

479. The oligo- or polydeoxyribonucleotide of claim 478, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

480. The oligo- or polydeoxyribonucleotide of claim 478, wherein the sugar moiety of said terminal nucleotide has oxygen atoms at each of the 2' and 3' positions thereof.

481. The oligo- or polydeoxyribonucleotide of claim 454, comprising at least one ribonucleotide.

482. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1′ position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

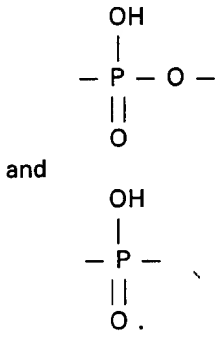
wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

483. The oligo- or polydeoxyribonucleotide of claim 482, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotde self-signaling or self-indicating or self-detecting.

484. The oligo- or polyd oxyribonucleotid of claim 482, wherein said Sig moiety comprises at least three carbon atoms.

485. The oligo- or polydeoxyribonucleotide of claim 482, wherein said covalent attachment is selected from the group consisting of



and

486. The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

487. The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

488. The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage comprises an allylamine group.

489. The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage comprises or includes an olefinic bond at the α-position relative to the point of attachment to x, y or z, or any of the moieties:

$$-CH=CH_2-NH-$$

$$-CH=CH-CH_2-NH-$$

$$-CH=CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-NH-,$$

$$-S-,\quad -\overset{\displaystyle O}{\overset{\|}{C}}-O,\text{ and } -O-.$$

490. The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

491. The oligo- or polydeoxyribonucleotide of claim 482, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and said Sig moiety is covalently attached to either or both of said x and y a phosphorus atom or phosphate oyxgen.

492. The oligo- or polydeoxyribonucleotide of claim 482, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme or an enzyme component, a hormone or a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten and an antibody or an antibody component, or a combination of any of the foregoing.

493. The oligo- or polydeoxyribonucleotide of claim 492, wherein said electron dense component comprises ferritin.

494. The oligo- or polydeoxyribonucleotide of claim 482, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein.

495. The oligo- or polydeoxyribonucleotide of claim 492, wherein said magnetic component comprises magnetic oxide.

496. The oligo- or polydeoxyribonucleotide of claim 495, wherein said magnetic oxide comprises ferric oxide.

497. The oligo- or polydeoxyribonucleotide of claim 492, wherein said enzyme or enzyme component is selected from the group consisting of alkaline phosphatase, acid phosphatase, β-galactosidase, ribonuclease, glucose oxidase and peroxidase.

498. The oligo- or polydeoxyribonucleotide of claim 492, wherein said metal-containing component is catalytic.

499. The oligo- or polydeoxyribonucleotide of claim 492, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

500. The oligo- or polydeoxyribonucleotide of claim 492, wherein Sig is selected from the group consisting of an antigen or hapten capable of complexing with an antibody or antibody component specific thereto, and an antibody or antibody component capable of complexing with an antigen or hapten.

501. The oligo- or polydeoxyribonucleotide of claim 482, wherein said oligo- or polydeoxyribonucleotide is terminally ligated or attached to a polypeptide.

502. A composition comprising the oligo- or polydeoxyribonucleotide of claim 482, a polypeptide capable of forming a complex with Sig and a moiety which can be detected when such complex is formed.

503. The composition of claim 500, wherein said polypeptide comprises polylysine.

504. The composition of claim 502, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

505. The composition of claim 502, wherein said Sig is a ligand and said polypeptide is an antibody thereto.

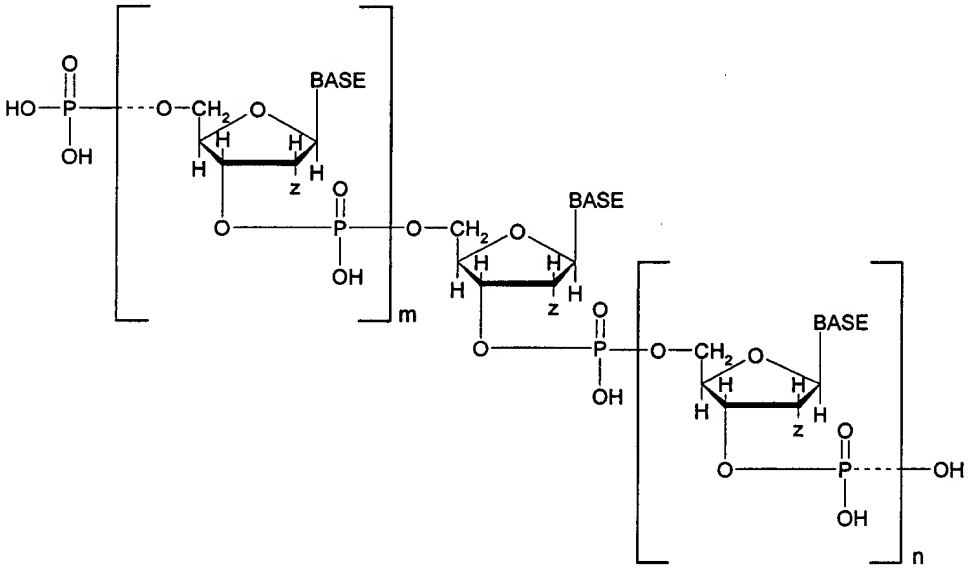
506. The oligo- or polydeoxyribonucleotide of claim 482, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

507. The oligo- or polydeoxyribonucleotide of claim 506, wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

508. The oligo- or polydeoxyribonucleotide of claim 506, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

509. The oligo- or polydeoxyribonucleotide of claim 482, comprising at least one ribonucleotide.

510. The oligo- or polydexoyribonucleotide of claim 482, having the structural formula:



, wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

511. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the formula

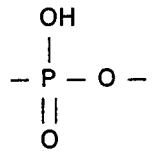
Sig – PM – SM – BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

512. The oligo- or polynucleotide of claim 511, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

513. The oligo- or polynucleotide of claim 511, wherein said Sig moiety comprises at least three carbon atoms.

514. The oligo- or polynucleotide of claim 511, wherein said covalent attachment is selected from the group consisting of



and

515. The oligo- or polynucleotide of claim 511, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

516. The oligo- or polynucleotide of claim 511, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a -CH_2NH- moiety, or both.

517. The oligo- or polynucleotide of claim 511, wherein said chemical linkage comprises an allylamine group.

518. The oligo- or polynucleotide of claim 511, wherein said chemical linkage comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties:

$$-CH=CH_2-NH-$$

$$-CH=CH-CH_2-NH-$$

$$-CH=CH-CH_2-O-CH_2-\underset{\underset{OH,}{|}}{CH}-CH_2-NH-,$$

$$-S-,\quad -\overset{\overset{O}{\|}}{C}-O,\text{ and }-O-.$$

519. The oligo- or polynucleotide of claim 511, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

520. The oligo- or polynucleotide of claim 511, wherein said PM is a monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or a phosphate oxygen.

521. The oligo- or polynucleotide of claim 511, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme or an enzyme component, a hormone or a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten and an antibody or an antibody component, or a combination of any of the foregoing.

522. The oligo- or polynucleotide of claim 521, wherein said electron dense component comprises ferritin.

523. The oligo- or polynucleotide of claim 511, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein.

524. The oligo- or polynucleotide of claim 521, wherein said magnetic component comprises magnetic oxide.

525. The oligo- or polynucleotide of claim 524, wherein said magnetic oxide comprises ferric oxide.

526. The oligo- or polynucleotide of claim 521, wherein said enzyme or enzyme component is selected from the group consisting of alkaline phosphatase, acid phosphatase, β-galactosidase, ribonuclease, glucose oxidase and peroxidase.

527. The oligo- or polynucleotide of claim 521, wherein said metal-containing component is catalytic.

528. The oligo- or polynucleotide of claim 521, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

529. The oligo- or polynucleotide of claim 521, wherein Sig is selected from the group consisting of an antigen or hapten capable of complexing with an antibody or antibody component specific thereto, and an antibody or antibody component capable of complexing with an antigen or hapten.

530. The oligo- or polynucleotide of claim 511, wherein said oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

531. A composition comprising the oligo- or polynucleotide of claim 511, a polypeptide capable of forming a complex with Sig and a moiety which can be detected when such complex is formed.

532. The composition of claim 531, wherein said polypeptide comprises polylysine.

533. The composition of claim 531, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

534. The composition of claim 531, wherein said Sig is a ligand and said polypeptide is an antibody thereto.

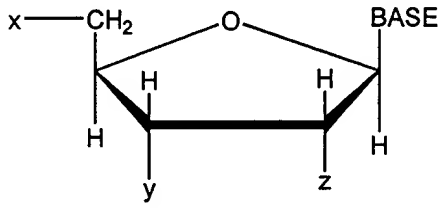
535. The oligo- or polynucleotide of claim 511, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polynucleotide.

536. The oligo- or polynucleotide of claim 535, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

537. The oligo- or polynucleotide of claim 535, wherein the sugar moiety of said terminal nucleotide has an oxygen atom at each of the 2' and 3' positions thereof.

538. The oligo- or polynucleotide of claim 511, comprising at least one deoxyribonucleotide.

539. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1′ position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate;

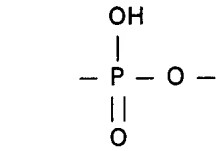
wherein z is selected from the group consisting of H— , HO— , a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3′ terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

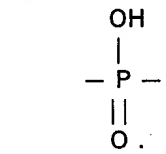
540. The oligo- or polynucleotide of claim 539, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

541. The oligo- or polynucleotide of claim 539, wherein said Sig moiety comprises at least three carbon atoms.

542. The oligo- or polynucleotide of claim 539, wherein said covalent attachment is selected from the group consisting of



and



543. The oligo- or polynucleotide of claim 539, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

544. The oligo- or polynucleotide of claim 539, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a -CH_2NH- moiety, or both.

545. The oligo- or polynucleotide of claim 539, wherein said chemical linkage comprises an allylamine group.

546. The oligo- or polynucleotide of claim 539, wherein said chemical linkage comprises or includes an olefinic bond at the α-position relative to x, y or z, or any of the moieties:

$$-CH=CH_2-NH-$$

$$-CH=CH-CH_2-NH-$$

$$-CH=CH-CH_2-O-CH_2-\underset{\displaystyle OH,}{\underset{|}{CH}}-CH_2-NH-,$$

$$-S-,\quad -\overset{\displaystyle O}{\overset{\|}{C}}-O,\text{ and }-O-.$$

547. The oligo- or polynucleotide of claim 539, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

548. The oligo- or polynucleotide of claim 539, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and Sig moiety is covalently attached to either or both of said x and y a phosphorus atom or a phosphate oxygen.

549. The oligo- or polynucleotide of claim 539, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme or an enzyme component, a hormone or a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten and an antibody or an antibody component, or a combination of any of the foregoing.

550. The oligo- or polynucleotide of claim 549, wherein said electron dense component comprises ferritin.

551. The oligo- or polynucleotide of claim 539, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein.

552. The oligo- or polynucleotide of claim 549, wherein said magnetic component comprises magnetic oxide.

553. The oligo- or polynucleotide of claim 552, wherein said magnetic oxide comprises ferric oxide.

554. The oligo- or polynucleotide of claim 549, wherein said enzyme or enzyme component is selected from the group consisting of alkaline phosphatase, acid phosphatase, β-galactosidase, ribonuclease, glucose oxidase and peroxidase.

555. The oligo- or polynucleotide of claim 549, wherein said metal-containing component is catalytic.

556. The oligo- or polynucleotide of claim 549, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

557. The oligo- or polynucleotide of claim 549, wherein Sig is selected from the group consisting of an antigen or hapten capable of complexing with an antibody or antibody component specific thereto, and an antibody or antibody component capable of complexing with an antigen or hapten.

558. The oligo- or polynucleotide of claim 539, wherein said oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

559. A composition comprising the oligo- or polynucleotide of claim 539, a polypeptide capable of forming a complex with Sig and a moiety which can be detected when such complex is formed.

560. The composition of claim 559, wherein said polypeptide comprises polylysine.

561. The composition of claim 559, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

562. The composition of claim 559, wherein said Sig is a ligand and said polypeptide is an antibody thereto.

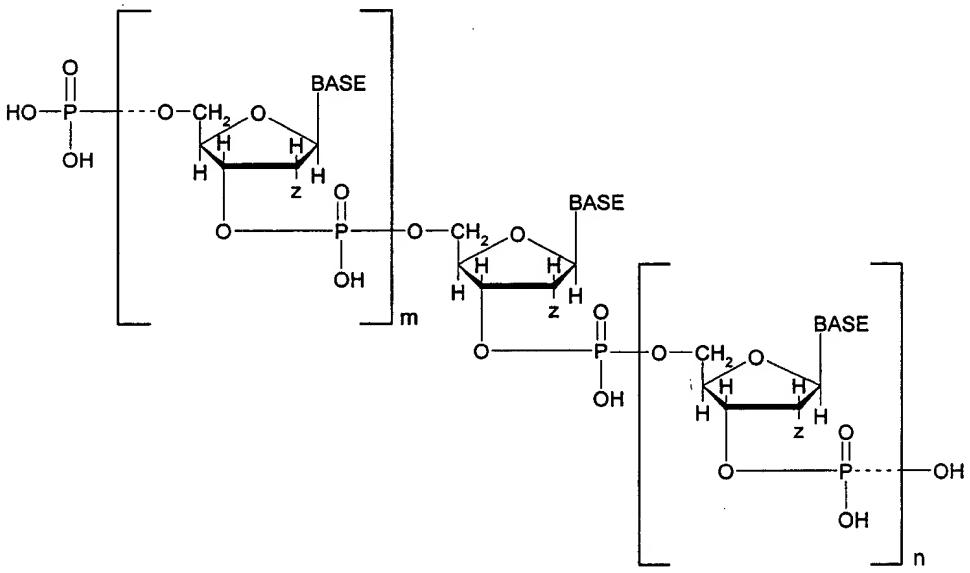
563. The oligo- or polynucleotide of claim 539, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polynucleotide.

564. The oligo- or polynucleotide of claim 563, wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

565. The oligo- or polynucleotide of claim 563, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

566. The oligo- or polynucleotide of claim 539, comprising at least one deoxyribonucleotide.

567. The oligo- or polynucleotide of claim 539, having the structural formula:



, wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

* * * * * * *